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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/828,920	04/20/2004	John C. Reed	066821-0281	6166

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EXAMINER
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ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/828,920	REED, JOHN C.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *1-4,7,8,10 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *5, 6 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Applicant's response of May 14, 2007, to the non-final action dated November 14, 2006 has been entered. Claims 1-11 are pending in the application. Claims 5 and 9 have been amended. No claims have been cancelled or newly added. Claims 1-4, 7, 8, 10 and 11 remain withdrawn from consideration, with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01. Claims 5, 6 and 9 are currently under examination.

Title of the Invention

The title of the invention has been changed to omit the word "Novel" at the beginning of the title. As stated in MPEP 606: Inasmuch as the words >"new,"< "improved," "improvement of," and "improvement in" are not considered as part of the title of an invention, these words should not be included at the beginning of the title of the invention and will be deleted when the Office enters the title into the Office's computer records, and when any patent issues. >

Response to Failure to Comply with 37CFR §1.821-1.825

The disclosure of the application was objected to in the previous office action of November 14, 2006, as lacking SEQ ID NOS for the amino acid sequences recited in the sequence alignments of Figures 1D and 1E. In view of Applicants' amendment of the brief description of the drawings for Figures 1D and 1E.b to refer to the sequences by appropriate SEQ ID NOS, the previous objection is hereby withdrawn.

Response to Claim Rejections - 35 USC § 112 – Written Description

Claims 5, 6 and 9 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The rejection set forth on pp. 4-5 of the previous office action dated November 14, 2006 is maintained for claims 5, 6 and 9 for reasons of record.

Applicant disagrees with rejection, arguing that the specification teaches that a NAC can associate and bind relatively specifically to a protein to form a bound complex, and that an agent is a chemical or biological molecule that has the potential to alter the association of a NAC with NAP, or a heterologous protein or self-association; that the agent is effective at modulating transcription mediated by NFκB. Moreover, the specification teaches assay methods for identifying agents that modulate NAC activity, that include for example, yeast two hybrid and *in vitro* binding assays, thus providing sufficient description and guidance for the claimed composition and methods. Applicant's arguments have been fully considered, but are not found persuasive.

As set forth in the previous office action, the instant claims embrace a large genus of NAC modulating agents that are therapeutic, and include simple or complex organic molecules, oligonucleotides and peptide-mimetics (paragraph [00118], p. 38) yet to be discovered, having the ability to alter a multitude of transcription activities and modulate apoptosis and treat numerous pathologies characterized by abnormal proliferation or abnormal inflammation. However, the specification fails to disclose any examples of the numerous non-protein agents that may be described as effective in modulating the association of NAC and NAP proteins. The specification does not describe the structure or functional nature of any non-protein agents that may be described as NAC modulating agents that are further therapeutic in numerous pathologies. The specification, while disclosing the association of various NAC and NAP proteins, fails to provide any examples for agents that modulate said association. Thus, the person of skill in the art could not predict that Applicant possessed any species of NAC modulating agents that constitute a therapeutic composition. Disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 (written description requirement not satisfied by merely providing "a result that one might achieve if one made that invention"); *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming a rejection for lack of written description because the specification does "little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate").

Therefore, the rejection of claims 5, 6 and 9 is maintained for reasons of record and the foregoing discussion.

Response to Claim Rejections - 35 USC § 112 - Lack of Enablement

Claims 5, 6 and 9 stand rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement. The rejection set forth on pp. 6-10 of the previous office action dated November 14, 2006 is maintained for claims 5, 6 and 9 for reasons of record.

Applicant disagrees with the rejection, reiterating the argument summarized above and further stating that the unpredictability discussed on page 8 of the previous office action relating to the different results observed between the yeast two hybrid system and that observed in 293T cell transfection provides no basis for the unpredictability in the yeast two hybrid system, because the yeast two hybrid assays were performed with the CARD domains of NAC ($CARD_L$), found to interact with capase-9 whereas the full length NAC failed to bind to caspase-9 in the 293 T cells. Applicants' arguments have been fully considered, but are not found persuasive.

It should be noted that the instant claims are drawn to a therapeutic NAC modulating agent that alters the association of NAP proteins. The instant claims contain no limitation as to the composition of the NAC associated protein (NAP) and thus encompass any CARD domain containing protein. The observation that the $CARD_L$ domain of NAC interacts with the CARD domains of caspase-9 in the yeast two hybrid system, but that full length NAC fails to interact with caspase-9 in 293T cells is highly relevant to the predictive ability of the yeast two hybrid system in relation to CARD domain proteins and thus also for identification of a NAC modulating agent in the two hybrid system.

In addressing the therapeutic composition of claim 5, Applicant argues that the composition comprises an effective amount of a NAC modulating agent that alters association of NAC and NAP proteins and the specification teaches an "effective amount" is a predetermined amount calculated to achieve the desired therapeutic effect. The specification also teaches the treatment of various pathologies using therapeutic compositions, and accordingly the specification provides sufficient description and guidance to enable the therapeutic compositions claimed.

Such is not found persuasive, because Applicant's response fails to address the various issues raised in the previous office action. Namely, the instant specification does not provide an

enabling disclosure for identifying a NAC modulating agent (that is not a NAC protein or an anti-NAC antibody) that is able to alter the association of NAC and NAP proteins, or alter transcription. The specification does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because the description fails to provide any examples of an effective agent, or guidance wherein an agent may specifically alter the association of NAC and NAP proteins *in vitro* or *in vivo*. The specification does not disclose any instances where NAC and NAP altered association or dissociation are involved in the regulation of transcription of any gene. Each of the Examples provided, involve the association of a NAC and NAP protein and assays showing said association. No dissociation of NAC and NAP proteins is described in any of the examples. The prior art is further silent on the description of an agent that is effective in the specific altered association or dissociation of NAC and NAP proteins. Thus, a person of skill in the art would therefore have to engage in additional experimentation to define conditions wherein NAC and NAP associations would be altered *in vitro* or *in vivo*, and further employ a screening procedure to identify and characterize an effective agent. Such further experimentation is regarded as undue and unpredictable, in view of the absence of sufficient guidance in either the instant specification or the prior art. Applicants should further note that claim 5 is a product by process claim that is at once directed to both a composition and a method of making said composition (see MPEP 2173.05(p) II).

Additionally, the specification is not enabling for a therapeutic composition comprising any NAC modulating agent, and a method of treating a pathology characterized by abnormal cell proliferation or abnormal inflammation by administering an effective amount of said NAC modulating composition. As previously indicated, NAC proteins exert numerous pleiotropic effects (including opposite effects) in an organism. For example, the specification states: "In addition to their role in caspase-activation, CARD domains have been implicated in other cellular processes. Some Card-containing proteins, for example, induce activation of the transcription factor NF-κB ...Card domains are found in some proteins that inhibit rather than activate caspases, such as the IAP..." although caspase activation resulting from CARD domain interactions is often involved in inducing apoptosis, other caspases are primarily involved in

proteolytic processing and activation of inflammatory cytokines (such as pro-IL-1α and pro-IL-18)." (paragraph [0028], p. 10). The specification further states: "In a normal cell, a steady level of association of NAP and NAC proteins likely occurs. This steady state level of association of NAP and NAC proteins in a particular cell type can determine the level of apoptosis in that cell type." (paragraph [00165, p. 54). Therefore, it is unclear how a NAC modulating agent (once identified), would be administered in an effective amount to treat a pathology without affecting normal cells in a patient, where said administration would disrupt the normal steady state level of association of NAP and NAC proteins. Applicant has failed to respond to the foregoing issue.

As previously stated, the instant specification is devoid of any actual data regarding either an effective NAC modulating agent, or instances wherein said agent is used as a therapeutic composition for treating any of the numerous pathologies that are characterized by abnormal cell proliferation (encompassing diverse conditions from psoriasis to cancer) or abnormal inflammation (encompassing diverse conditions from asthma to arthritis). Moreover, a NAC modulating agent that is an antagonist of a specific NAC-NAP association, may have a deleterious effect in a disease state requiring such association. For example, a cancer treatment using an antagonist agent would likely be ineffective and may serve to increase disease severity by decreasing apoptosis. Additionally, the post-filing art of Ferreira et al. (Clin. Cancer Res. 8:2024-2034; 2002) states: "As far as proapoptotic strategies are concerned, toxicity may represent the potential obstacle to successful clinical development. These approaches are not necessarily based on structural differences between normal and cancer cells. Therefore, achieving tumor cell specificity, while minimizing toxicity, will probably be the major challenge in the development of this type of approach. Tumor cell specificity is not the major concern for apoptosis-permissive strategies, which mainly target cancer cell specific alterations. However, the mechanisms by which apoptosis is facilitated are, thus far, mostly unclear, and only a better mechanistic understanding will allow a more effective exploitation of this secondary apoptotic effect during clinical trials. In general, because of mutations/alterations in the apoptotic machinery, solid tumors have often lost the capacity to undergo instantaneous and massive apoptosis" (first column, p. 2030). Applicant has also failed to respond to the foregoing issue.

Therefore, the rejection of claims 5, 6 and 9 is maintained for reasons of record and the foregoing discussion.

Response to Claim Rejections - 35 USC § 112- Second Paragraph

Claim 9 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite, in the previous office action dated November 14, 2006. In view of Applicant's amendment of the claim introducing language limiting transcription to NFκB, and upon further consideration, the previous rejection is hereby withdrawn.

Conclusion

Claims 5, 6 and 9 are not allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR§1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst William Phillips, whose telephone number is **(571) 272-0548**. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00-4:00 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

For all other customer support, please call the USPTO Call Center (UCC) at **(800) 786-9199**.

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